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Hepcidin and Iron in Global Health (HIGH)

Submission date
19/06/2014

Recruitment status
No longer recruiting

Registration date
16/07/2014

Overall study status
Completed

Last Edited
16/12/2022

Condition category
Haematological Disorders

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Iron deficiency anaemia is a medical condition that happens when a lack of iron results in fewer red blood cells being made by the body. Red blood cells carry and store oxygen in the blood and if there are fewer around than normal the organs will not get as much oxygen as usual. This can cause people to become pale and tired, short of breath, have heart palpitations and children may fail to thrive. In low-income (developing) countries, 50% or more of young children suffer from iron deficiency. The World Health Organisation (WHO) has recommended that in countries where more than 40% have anaemia, all young children should be given iron supplements. However, large studies have revealed that giving large doses of iron to young children in areas where there are a high number of infections is risky. Some research suggests that increasing the amount of iron in the body means that more is available to the pathogen as well and this could make the infection worse. Taking this into account, iron supplements should only be given to children when they need it and are best able to use it. However, in areas of high infection, it can be difficult to determine when its best to give a child iron supplements. Hepcidin is a recently discovered hormone that is thought to indicate whether it is safe for someone to take iron. In this study, we hope to find out whether hepcidin can be used to give iron to children more safely.

Who can participate?
Healthy, young children, aged 6-23 months, coming to participating Reproductive and Child Health Clinics (RCH) in Gambia

What does the study involve?
After taking an initial sample of blood and testing it to make sure they are healthy, participants are randomly allocated to one of three groups and take part in the study for 12 weeks. Those in group A (the reference group) are given a micronutrient powder (MNP) containing 12 mg/day iron. Those in group B are given the MNP containing 12 mg/day iron or 0 mg/day iron based on a weekly hepcidin screening to tell if iron should be given for the next 7 days or not. Those in group C are given MNP containing 6 mg/day iron or 0 mg/day iron based on a weekly hepcidin screening to tell if iron should be given for the next 7 days or not. Each week, finger prick blood samples will be taken to find out the hepcidin level, haemoglobin (Hb) level and test for malaria. After the 12 weeks , 2 additional blood samples and 3 stool samples are taken. Morbidity (a measure of how healthy a participant is) is assessed twice a week.

What are the possible benefits and risks of participating?
Benefits will include study participants having access to basic medical services for free. Participants will benefit from daily monitoring by qualified field workers. Anaemia and malaria can also be diagnosed and managed. There are risks associated with a large intake of iron supplements. However, the reference group of this study takes iron as per the recommendation of the World Health Organization and the other two groups take an overall lower dose of iron. If those in group C are moderately anaemic (borderline severe anaemia), they may be at risk of receiving too little iron but will be monitored every week and if seen to become severely anaemic, will be treated as per Gambia Government recommendation for management of severe anaemia. The MNP (MixMe WHO) is distributed by UNICEF and by the World Food Programme and has been used successfully in a number of studies in developing countries. No emergency is expected to result from taking this supplement. However, a nurse will always be available who will decide whether to refer a participant to a health facility in case this is necessary.

Where is the study run from?
This study will be run from 12 communities in Jarra West and Kiang East of Rural Gambia.

When is the study starting and how long is it expected to run for?
May 2014 to November 2015

Who is funding the study?
Medical Research Council (MRC) (UK) and the Bill & Melinda Gates Foundation (USA)

Who is the main contact?
Dr Rita Wegmüller
rwegmuller@mrc.gm

Contact information

Type(s)
Scientific

Contact name
Dr Rita Wegmüller

Contact details
Head of Station, MRC Keneba
MRC International Nutrition Group
MRC Keneba
MRC Unit, The Gambia
Banjul
Gambia
PO Box 273
-
rwegmuller@mrc.gm

Additional identifiers

Protocol serial number
SCC 1358 Version 1

Study information

Scientific Title
Efficacy and safety of hepcidin-based screen-and-treat approaches using two different doses vs a standard universal approach of iron supplementation in young children in rural Gambia: a double-blind randomized controlled trial

Acronym
HIGH

Study objectives
A screen-and-treat approach to iron supplementation in young children will achieve similar efficacy in combating iron deficiency and iron deficiency anaemia at a lower overall dosage of iron which will improve safety and tolerability of iron supplementation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Gambia Government/MRC Joint Ethics Committee, 19/12/2013, ref. SCC 1358v1

Study design
Proof-of-concept three-arm double-blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Anaemia

Interventions
The participants will be randomly assigned (1:1:1 ratio) to either receive:
1. MNP containing 12 mg/day iron
2. MNP containing 12 mg/day iron or 0 mg/day iron based on a weekly hepcidin screening indicating if iron can be given for the next 7 days or not
3. MNP containing 6 mg/day iron or 0 mg/day iron based on a weekly hepcidin screening indicating if iron can be given for the next 7 days or not

Intervention product
The nutritional supplement to be used in this trial is a micronutrient powder (MNP) (MixMe WHO) also distributed by UNICEF and WFP. The MNP contains 15 micronutrients. Three investigational products containing different quantities of iron will be administered:
1. MNP with 12 mg iron
2. MNP with 6 mg iron
3. MNP with 0 mg iron

Intervention Type

Supplement

Primary outcome(s)
Haemoglobin concentration at study day 84

Key secondary outcome(s))
1. Proportion of anaemia at study day 84
2. Proportion of iron deficiency at day 84
3. Proportion of iron deficiency anaemia at day 84
4. Iron dosage
5. Morbidity
6. Safety
7. Amount of iron absorbed over the supplementation period

Completion date
30/11/2015

Eligibility

Key inclusion criteria
1. Apparently healthy
2. Age: 6 to 23 months
3. Not severely malnourished (HAZ, WAZ >-3 SD and WHZ > -2 SD)
4. Hb ≥ 7 g/dL and < 11 g/dL
5. Free of malaria
6. Resident in the study area
7. Ability and willingness to comply with the study protocol (weekly study visits with finger prick blood sampling)
8. Informed consent given by parent or guardian

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 months

Upper age limit
23 months

Sex
All

Key exclusion criteria

1. Congenital disorders
2. Chronic disease
3. Regular medication
4. Currently participating in another study

Date of first enrolment
26/05/2014

Date of final enrolment
30/11/2015

Locations

Countries of recruitment
Gambia

Study participating centre
MRC Keneba
Banjul
Gambia
PO Box 273

Sponsor information

Organisation
Medical Research Council (MRC) (UK)

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2016		Yes	No
Results article		01/01/2023	16/12/2022	Yes	No
Protocol article	protocol	01/09/2016		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes